

WHAT IS CLAIMED IS:

5        1. An isolated fusion molecule comprising a first polypeptide sequence capable of specific binding to a native IgG inhibitory receptor comprising an immune receptor tyrosine-based inhibitory motif (ITIM), expressed on mast cells, basophils or B cells, functionally connected to a second polypeptide sequence capable of specific binding, directly or indirectly, to a native IgE receptor (Fc $\epsilon$ R).

10        2. The fusion molecule of claim 1 wherein said inhibitory receptor is a low-affinity IgG receptor Fc $\gamma$ RIIb.

15        3. The fusion molecule of claim 2 wherein said IgE receptor is a high-affinity Fc $\epsilon$ RI receptor.

20        4. The fusion molecule of claim 2 wherein said IgE receptor is a low-affinity IgE receptor Fc $\epsilon$ RII (CD23).

25        5. The fusion molecule of claim 3 wherein said Fc $\gamma$ RIIb and Fc $\epsilon$ RI receptors are of human origin.

30        6. The fusion molecule of claim 4 wherein said Fc $\gamma$ RIIb and Fc $\epsilon$ RII receptors are of human origin.

15        7. The fusion molecule of claim 1 wherein said second polypeptide sequence is capable of specific binding directly to said native IgE receptor.

20        8. The fusion molecule of claim 7 wherein said native IgE receptor is a high-affinity Fc $\epsilon$ RI receptor.

25        9. The fusion molecule of claim 7 wherein said native IgE receptor is a low-affinity Fc $\epsilon$ RII receptor (CD23).

30        10. The fusion molecule of claim 1 wherein said second polypeptide sequence is capable of specific binding to said native IgE receptor through a third polypeptide sequence.

15        11. The fusion molecule of claim 10 wherein said native IgE receptor is a high-affinity Fc $\epsilon$ RI receptor.

20        12. The fusion molecule of claim 10 wherein said native IgE receptor is a low-affinity Fc $\epsilon$ RII receptor (CD23).

25        13. The fusion molecule of claim 10 wherein said second polypeptide sequence comprises an allergen sequence.

14. The fusion molecule of claim 13 wherein said allergen sequence is that of a food allergen.

15. The fusion molecule of claim 14 wherein said food allergen is selected from the group consisting of peanut, shellfish, milk, fish, soy, wheat, egg and tree nut allergens.

5 16. The fusion molecule of claim 13 wherein said allergen sequence is that of a pollen allergen.

17. The fusion molecule of claim 13 wherein said IgE receptor is a high-affinity Fc $\epsilon$ RI receptor.

10 18. The fusion molecule of claim 13 wherein said native IgE receptor is a low-affinity Fc $\epsilon$ RII receptor (CD23).

19. The fusion molecule of claim 13 wherein said IgG inhibitory receptor is a low-affinity Fc $\gamma$ RIIb receptor.

20. The fusion molecule of claim 19 wherein said IgE receptor is a high-affinity Fc $\epsilon$ RI receptor.

15 21. The fusion molecule of claim 20 wherein said Fc $\gamma$ RIIb and Fc $\epsilon$ RI receptors are of human origin.

22. The fusion molecule of claim 1 or claim 10 wherein said first and second polypeptide sequences are connected through a linker.

23. The fusion molecule of claim 22 wherein said linker is a polypeptide sequence.

20 24. The fusion molecule of claim 23 wherein said polypeptide sequence consists of 5 to 25 amino acid residues.

25 25. The fusion molecule of claim 23 wherein said polypeptide sequence consists of 10 to 25 amino acid residues.

26. The fusion molecule of claim 23 wherein said polypeptide sequence consists of 15 to 25 amino acid residues.

27. The fusion molecule of claim 1 wherein said first and second polypeptide sequences are directly fused to each other.

28. The fusion molecule of claim 10 wherein said first and second polypeptide sequences are directly fused to each other.

29. The fusion molecule of claim 3 wherein said first polypeptide comprises an amino acid sequence having at least 90% sequence identity with the hinge-CH<sub>2</sub>-CH<sub>3</sub> portion of an IgG immunoglobulin heavy chain constant region

5 30. The fusion molecule of claim 29 wherein said immunoglobulin is selected from the group consisting of IgG<sub>1</sub>, IgG<sub>2</sub>, IgG<sub>3</sub> and IgG<sub>4</sub>.

31. The fusion molecule of claim 30 wherein said IgG is IgG<sub>1</sub>.

10 32. The fusion molecule of claim 31 wherein said first polypeptide comprises an amino acid sequence having at least 90% sequence identity with the amino acid sequence of SEQ ID NO: 3.

33. The fusion molecule of claim 31 wherein said first polypeptide has at least 90% sequence identity with the amino acid sequence of SEQ ID NO: 3.

15 34. The fusion molecule of claim 29 wherein said second polypeptide comprises an amino acid sequence having at least 90% sequence identity with the CH<sub>2</sub>-CH<sub>3</sub>-CH<sub>4</sub> portion of an IgE immunoglobulin heavy chain constant region.

20 35. The fusion molecule of claim 34 wherein said second polypeptide comprises an amino acid sequence having at least 90% sequence identity with the amino acid sequence of SEQ ID NO: 6.

36. The fusion molecule of claim 34 wherein said second polypeptide has at least 90% sequence identity with the amino acid sequence of SEQ ID NO: 6.

25 37. The fusion molecule of claim 29 wherein said second polypeptide comprises an amino acid sequence having at least 90% sequence identity with the amino acid sequence of a native allergen.

38. The fusion molecule of claim 37 wherein said second polypeptide has at least 90% sequence identity with the amino acid sequence of a native allergen.

25 39. The fusion molecule of claim 37 wherein said second polypeptide has at least 90% sequence identity with any of SEQ ID NOS: 8-173.

30 40. The fusion molecule of claim 3 wherein said first polypeptide sequence comprises a sequence encoded by nucleic acid hybridizing under stringent conditions to the complement of the hinge-CH<sub>2</sub>-CH<sub>3</sub> coding sequence of SEQ ID NO: 1, wherein said first polypeptide sequence is capable of specific binding to a native human Fc $\gamma$ RIIb receptor.

41. The fusion molecule of claim 3 wherein said second polypeptide sequence comprises a sequence encoded by nucleic acid hybridizing under stringent conditions to the complement of the CH2-CH3-CH4 coding sequence of SEQ ID NO: 4, wherein said second polypeptide sequence is capable of specific binding to a native human Fc $\epsilon$ RI receptor.

5 42. A single-chain fusion molecule comprising a first polypeptide sequence having at least 90% sequence identity with the amino acid sequence of SEQ ID NO: 3 and capable of specific binding to a native human Fc $\gamma$ RIIb receptor, functionally connected to a second polypeptide sequence having at least 90% sequence identity with the amino acid sequence of SEQ ID NO: 6 and capable of specific binding, directly or indirectly, to a native human Fc $\epsilon$ RI receptor.

10 43. The fusion molecule of claim 42 wherein said first polypeptide sequence comprises at least part of the CH2 and CH3 domains of a native human IgG<sub>1</sub> constant region.

44. The fusion molecule of claim 43 wherein said first polypeptide sequence additionally comprises at least part of the hinge of a native human IgG<sub>1</sub> constant region.

15 45. The fusion molecule of claim 44 wherein said first polypeptide sequence comprises at least part of the hinge, CH2 and CH3 domains of a native human IgG<sub>1</sub> heavy chain constant region, in the absence of a functional CH1 region.

46. The fusion molecule of claim 45 wherein said first polypeptide sequence consists of the hinge, CH2 and CH3 domains of a native human IgG<sub>1</sub> heavy chain constant region.

20 47. The fusion molecule of claim 42 wherein said second polypeptide sequence comprises at least part of the CH2, CH3, and CH4 domains of a native human IgE heavy chain constant region.

48. The fusion molecule of claim 47 wherein said second polypeptide sequence consists of the CH2, CH3 and CH4 domains of a native human IgE heavy chain constant region.

25 49. The fusion molecule of claim 48 wherein said second polypeptide sequence is functionally connected to a first polypeptide sequence consisting of the hinge, CH2 and CH3 domains of a native human IgG<sub>1</sub> heavy chain constant region sequence through a polypeptide linker.

50. The fusion molecule of claim 49 wherein said polypeptide linker consists of 5 to 25 amino acid residues.

30 51. The fusion molecule of claim 50 wherein said polypeptide linker consists of 10 to 25 amino acid residues.

52. The fusion molecule of claim 51 wherein said polypeptide linker consists of 15 to 25 amino acid residues.

- 5           53. The fusion molecule of SEQ ID NO: 7. ✓  
54. A fusion molecule having at least 90% sequence identity with SEQ ID NO: 7. ✓  
55. An isolated nucleic acid molecule encoding a fusion molecule of claim 1.  
56. An isolated nucleic acid molecule encoding a fusion molecule of claim 23.  
57. An isolated nucleic acid molecule encoding a fusion molecule of claim 27.  
58. A vector comprising and capable of expressing a nucleic acid molecule of claim 56.  
59. A vector comprising and capable of expression a nucleic acid molecule of claim 57.  
10          60. A host cell transformed with the vector of claim 58.  
61. A host cell transformed with the vector of claim 59.  
62. A pharmaceutical composition comprising a fusion molecule of claim 1 in admixture with a pharmaceutically acceptable ingredient.

15          63. A pharmaceutical composition comprising a fusion molecule of claim 10 in admixture with a pharmaceutically acceptable ingredient.

16          64. An article of manufacture comprising a container, a fusion molecule of claim 1 within the container, and a label or package insert on or associated with the container.

17          65. The article of manufacture of claim 64 wherein said label or package insert comprises instructions for the treatment of an IgE-mediated biological response.

18          66. The article of manufacture of claim 65 wherein said biological response is a IgE-mediated hypersensitivity reaction.

19          67. The article of manufacture of claim 66 wherein said label or package insert contains instruction for the treatment of a condition selected from the group consisting of asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria, angioedema, and anaphylactic shock.

20          68. A method for the treatment of a condition associated with an IgE-mediated biological response, comprising administering an effective amount of a fusion molecule of claim 1 to a subject in need.

21          69. The method of claim 68 wherein said subject is a human patient.

22          70. The method of claim 69 wherein said condition is an IgE-mediated hypersensitivity reaction.

71. The method of claim 70 wherein said condition is selected from the group consisting of asthma, allergic rhinitis, atopic dermatitis, severe food allergies, chronic urticaria, angioedema, and anaphylactic shock.

72. The method of claim 68 wherein said administration is preventative prior to the onset of said biological response.  
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